December 14, 2023

Robert M. Califf M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993-0002

Submitted electronically via www.regulations.gov

Re: Quality Management Maturity Program for Drug Manufacturing Establishments; Establishment of a Public Docket; Request for Comments [Docket Number FDA-2023-N-3721]

Dear Commissioner Califf:

Premier Inc. appreciates the opportunity to respond to the Food and Drug Administration (FDA) on the request for comments titled *"Quality Management Maturity Program for Drug Manufacturing Establishments; Establishment of a Public Docket; Request for Comments [Docket Number FDA-2023-N-3721]",* which was published in the *Federal Register* on September 15, 2023. The FDA is soliciting public comment on the development of a Quality Management Maturity (QMM) program, which aims to improve manufacturing practices and curb drug shortages.

As a leader in addressing drug shortages for almost twenty years, Premier agrees with the FDA that greater focus on supplier quality incentives and rewards, including payment for reliably meeting providers' supply requirements, is key to incenting manufacturers to participate in healthy and sustainable pharmaceutical markets. However, ***Premier has serious concerns that a rating system like the QMM may generate unintended downstream consequences that exacerbate drug shortages and create new operational challenges for U.S. healthcare providers***.

Premier's comments focus on highlighting concerns with the QMM program as proposed and recommending alternate approaches to creating a gold standard for quality manufacturing, including fully implementing existing authorities to address drug shortages prior to establishing new programs.

I. BACKGROUND ON PREMIER INC. AND OUR LEADERSHIP IN ADDRESSING DRUG SHORTAGES

Premier is a leading healthcare improvement company, uniting an alliance of more than 4,350 U.S. hospitals and health systems and 300,000 continuum of care providers to transform healthcare. With integrated data and analytics, collaboratives, supply chain solutions, consulting and other services, Premier enables better care and outcomes at a lower cost. A 2006 Malcolm Baldrige National Quality Award recipient, Premier plays a critical role in the rapidly evolving healthcare industry, collaborating with providers to co-develop long-term innovations that reinvent and improve the way care is delivered to patients nationwide. A key component of Premier's alliance is our Integrated Pharmacy Program, which combines essential clinical data with purchasing power to deliver reduced costs, improved quality, safety and resiliency, and increased knowledge-sharing among healthcare professionals.

Premier has been a leader in addressing drug shortages for more than twenty years and is committed to eliminating drug shortages from both a policy perspective via legislative and regulatory action as well as pursuing actionable, market-based solutions. Premier's ProvideGx program identifies safe, high-quality supply sources for drugs that are or may be at risk of being added to the national drug shortage list. Guided by health systems with more than 1,600 hospitals across the nation, ProvideGx creates long-term committed buying contracts that provide participating manufacturers with the surety needed to increase

production. Premier's programs, including ProvideGx, currently provide hospitals access to more than 150 drugs that are or have been recently designated as shortage drugs.

Since 2020, Premier's drug shortage programs have:

- Successfully resolved 15 drug shortages, resulting in their official delisting from the FDA shortage list.
- Ensured uninterrupted supply of many shortage drugs despite demand spikes of more than 150 percent during the pandemic.
- Continued to bring resiliency to the market by incenting the domestic manufacture of vital drugs through investments in VGYAAN and Exela Pharma Sciences, which combined are working to bring new, domestic sources of 20 different shortage drugs and counting.

A key component to Premier's success in mitigating drug shortages is the stringent contracting and vetting process manufacturers who wish to work with Premier must undergo. This includes sharing information regarding the location of their finished dose manufacturing and active pharmaceutical ingredient (API) sources. In addition, all manufacturers participating in Premier programs are vetted to enable more geographically diverse production capability, adequate safety stocks and surge capabilities to meet sudden spikes in demand. Finally, manufacturers are asked to share their redundancy and contingency plans to ensure ongoing supply of product and mitigate risk. Premier maintains this level of information for almost 6,000 unique National Drug Codes (NDCs) and leverages the information to assign a supply chain resiliency risk score to each product. That score is then utilized by Premier and its hospital-led sourcing committees to make contracting decisions that are in the best interest of patient care and supply chain resiliency.

Premier's ongoing commitment to addressing drug shortages also includes diligent advocacy efforts over the years including serving as the lead proponent of the Mitigating Emergency Drug Shortages (MEDS) Act, which was incorporated and signed into law as part of the CARES Act in March 2020.

Premier will continue to innovate and collaborate across diverse stakeholders to address ongoing drug shortages.

II. THE FDA SHOULD FULLY IMPLEMENT EXISTING STATUTORY AUTHORITIES TO ADDRESS DRUG SHORTAGES PRIOR TO ESTABLISHING NEW PROGRAMS

In March 2020, Congress provided the FDA with several new statutory authorities to mitigate drug shortages as part of the CARES Act. Specifically, these provisions:

- Created a priority pathway for the review of drug shortage applications;
- Required a report examining national security risks as a result of drug shortages;
- Strengthened FDASIA Title X reporting requirements to include full disclosure of the problems resulting in a shortage, information concerning the extent of a shortage, its expected durations, and other information the Secretary may require;
- Extended FDASIA Title X reporting requirements to API manufacturers; and
- Required manufacturers to maintain redundancy and contingency plans to ensure ongoing supply.

Unfortunately, it has been more than three years since the passage of these provisions and FDA has yet to fully implement any of them. For example, FDA published draft guidance on risk management plans in June 2022 and updated FDASIA Title X reporting requirements in April 2023, but has yet to finalize them. Furthermore, in the FDA's recent report to Congress for FY 2022, the FDA notes the CARES provisions but does not speak to an implementation timeline or how the new authorities helped mitigate shortages.[1]

[1] FDA Annual Report to Congress for CY 2022. Available at: https://www.fda.gov/media/169302/download?utm_medium=email&utm_source=govdelivery

In addition, Premier has significant concerns that FDA is moving forward with implementing its new statutory authority in a manner that does not align with Congressional intent.[2] [3] For example, in passing the CARES Act, Congress intended to create upstream visibility into potential disruptions in the pharmaceutical supply chain and hold API manufacturers accountable for reporting discontinuances and interruptions to help mitigate potential downstream shortages as early as possible. In draft guidance, the FDA proposes passing this burden to finished-dose manufacturers who may not have proper visibility into API production, supply, or market share to determine early warning signals of a potential shortage – counter to the intent of the legislative language which is to hold manufacturers of API accountable for supply chain sustainability. Therefore, Premier urged FDA to reevaluate its interpretation of the CARES Act provisions and extend notification requirements regarding discontinuances and interruptions in the manufacturing of API to the manufacturer of the API itself.

Given the delays with the FDA implementing statutory authorities from 3+ years ago, Premier recognizes it is difficult to assess how prior laws are impacting drug shortages. Therefore, ***Premier urges the FDA to prioritize fully implementing its existing statutory authorities to address drug shortages prior to establishing new programs such as the QMM***. It is critical for FDA to fully implement its existing statutory authorities and reestablish a baseline for drug shortages. Understanding what is working and what outstanding gaps remain is essential before establishing new programs that may result in unintended consequences and unnecessary burden to the healthcare ecosystem with limited or no value.

III. THE QMM PROGRAM LACKS DETAILS AND INTRODUCES UNNECESSARY COMPLEXITY INTO THE HEALTHCARE ECOSYSTEM

The FDA recently formed a multidisciplinary working group on the QMM rating system, stating that ratings could provide intelligence on production facilities' performance and robustness, and support flexibility for manufacturers to make post-approval manufacturing changes with less regulatory oversight. However, currently lacking are the necessary details for operationalizing and implementing a rating system, including how ratings are managed and how facilities that receive any score under the top rating will be managed in the current regulatory environment. Per FDA's own admission in the QMM program proposal, while the working group has been meeting for over a year, there are several unintended consequences that need to be flushed out prior to implementing a QMM program, including but not limited to:

- Clearly defining the scope and meaning of QMM ratings
- Incentivizing purchasers to consider QMM in decision-making
- Separating QMM appraisals from regulatory compliance
- Relying on purchasers to understand their supply chains
- Understanding if FDA can disclose specific information about the drug product supply chain
- Researching the unintended consequences of QMM ratings, such as market over-consolidation
- Addressing potential risks of using QMM ratings in decision-making
- Addressing comparative quality decisions, liability, and risk to providers

For instance, such a system may be inherently subject to bias and proposes to assign a rating or ranking to every FDA-approved drug manufacturing *site* around the globe. Under this model, one single drug with the same dosage and strength produced by the same manufacturer with the same NDC, in theory, could accrue a different quality rating based on the specific facility at which it was produced – creating confusion, little parity and potentially the need for multiple labels to distinguish between the 5-star and 3-star "twin" products. Such a system may discourage manufacturers from creating diversification within their portfolios

[2] https://premierinc.com/downloads/Premier-Comments_FDA-Guidance-on-Risk-Management-Plans-to-Mitigate-Drug-Shortages.pdf
[3] https://premierinc.com/downloads/Premier-Comments_FDA-Guidance-on-Notifications-for-Supply-Disruptions-to-Mitigate-Drug-Shortages.pdf

and ensuring that products are manufactured at multiple sites – instead, it may encourage consolidation of manufacturing to a single site to avoid this conundrum, which is counter to addressing drug shortages.

A quality rating system can also unintentionally select winners and losers in an already-constrained environment – further increasing barriers to entry and discouraging competition. With the likelihood for pricing variability on high versus low-rated products, many lesser-rated manufacturers may make the difficult decision of reducing production or exiting the market entirely – two actions that can, and have, triggered drug shortages. Furthermore, such a rating system may exacerbate concerns with health equity if certain patients, payers, or providers can only afford to access lower rated products thereby potentially leading to equity challenges in low income or at-risk populations.

Another major challenge in a rating system approach is the complexity this can introduce into the pharmacy dispensing workflow. Much of this can be attributed to the confusion created by the distinct product quality labeling likely required and as noted earlier, but an added factor is payer preference considerations. For comparison, in the brand and generic drug space, if a generic is covered by a payer, all manufacturers of the generic drug are typically covered and can be interchanged by the pharmacist. Alongside specific quality ratings, many payers may only select a single rating or only higher-ranked products to place on formulary. This can result in the need for pharmacies to create extensive workflows to ensure the patient receives the right product and can create delays in patient care as pharmacists work to understand which product would be covered by each patient's individual insurance. This adds additional complexity in emergency situations where every second counts to administer necessary medications, and any operational delay can have detrimental effects on patient outcomes. A quality rating system may also inhibit healthcare providers from creating their own institutional formularies, which can lead to severe inefficiencies for a pharmacy to manage inventory effectively, especially given the expense of products and refrigerator space required for storage.

In addition to payer dynamics, what liability would exist to providers using a lower-rated drug? An example of how this applies in practice can be seen with biosimilars: hospitals cite confusion on how to address a situation when a patient receives the wrong manufacturer of a biosimilar due to confusion with payor coverage and a lack of interchangeability. The patient receives the correct molecule, but the wrong manufacturer. Hospitals are reporting these as medication errors, creating significant confusion for patients when they are informed that a medication error occurred, while they did receive the right drug at the right dose. A similar scenario can occur with quality ranked drugs – the FDA should establish clear recommendations regarding what would constitute a medication error for product of a particular quality rating.

Finally, it is important to note how drug shortages would be defined in the context of quality ratings. If a 5-star product is unavailable, can pharmacies substitute a lower rated product due to the shortage? Will the FDA drug shortage list be able to accommodate tracking and listing of shortages based on the quality rating?

Prior to moving forward, Premier urges the FDA to carefully consider the unintended consequences of the QMM program in potentially exacerbating drug shortages, worsening market dynamics, and increasing burden on the healthcare system. Until all the outstanding questions related to the program can be addressed, the FDA should halt further implementation. Should the FDA choose to proceed, Premier urges the FDA to establish a public-private collaboration to solicit additional feedback and better define the program details with the perspective of government, industry, healthcare providers, and patients represented. Furthermore, should a QMM program be pursued, Premier urges the FDA to consider a pilot phase prior to global rollout.

IV. THE GOLD STANDARD FOR QUALITY SHOULD BE TIMELY AND EQUITABLE FDA INSPECTIONS

Currently, the FDA assesses whether a facility is in a state of control through periodic inspections that provide an evaluation of manufacturing operations, including their system for quality management. ***Rather***

than creating a net-new ranking system, the quality standard should focus on FDA approval and inspection, with all FDA-registered global manufacturers inspected equitably and consistently via unannounced inspections at the same time intervals.

It is welcome news that the Fiscal Year (FY) 2023 Omnibus Appropriations Bill contains a provision requiring the FDA to establish a pilot program for unannounced foreign inspections, however, more must be done above and beyond a pilot program to hold both domestic and overseas manufacturers of finished dose forms and APIs to the same standard. One quality standard equally applied to all producers can encourage domestic investment and shorten supply chains. And importantly, it preserves the FDA as the gold standard for all medical product and food inspections, of which U.S. consumers already rely.

To level the playing field, the FDA will require the appropriate resources in highly trained and experienced inspectors and may also need additional statutory authority. Once a level playing field is adopted as policy, the FDA should provide a five-year plan, with metrics and annual targets to achieve the desired parity.

V. CONCLUSION

In closing, Premier appreciates the opportunity to submit comments to inform policymaking for drug shortages. Solutions that drive mature manufacturing quality systems are critical to address the symptoms of an unhealthy pharmaceutical market, pervasive drug shortages and the quality of care delivered to patients. While well intentioned, a quality ranking approach can usher in substantial unintended consequences that run counter to these goals.

Premier looks forward to continuing to work with the FDA to help prevent and resolve these shortages today and for the future. If you have any questions regarding our comments or need more information, please feel free to contact me at soumi_saha@premierinc.com or 732-266-5472.

Sincerely,

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